PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

THOMSON, Clive Beresford
GLAXOSMITHKLINE
Corporate Intellectual Property
980 Great West Road
Brentford
Middlesex TW8 9GS
GRANDE BRETAGNE

29 MAR 2004

AWP

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

	Date of mailing *(day/month/year)* 25.03.2004
Applicant's or agent's file reference AXP/PG4787	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP 03/03347	27.03.2003	28.03.2002

Applicant
GLAXO GROUP LIMITED et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Ullrich, J Tel. +49 89 2399-8048

Form PCT/IPEA/416 (January 2004)

Express Mail Label No.
EV332062821US

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference AXP/PG4787	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/03347	International filing date *(day/month/year)* 27.03.2003	Priority date *(day/month/year)* 28.03.2002
International Patent Classification (IPC) or both national classification and IPC C07D413/12		
Applicant GLAXO GROUP LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
30.09.2003	25.03.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Ousset, J-B Telephone No. +49 89 2399-8271

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/03347

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-84 as originally filed

Claims, Numbers

1-22 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 10-12,18

   because:

   ☒ the said international application, or the said claims Nos. 18 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 10-12 are so unclear that no meaningful opinion could be formed *(specify)*:

   see separate sheet

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:

   ☐ restricted the claims.

   ☒ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-9,13-17,19-22 (all part) .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-9,13-17,19-22 (all part)
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-9,13-17,19-22 (all part)
Industrial applicability (IA)	Yes:	Claims	1-9,13-17,19-22 (all part)
	No:	Claims	

2. Citations and explanations

   see separate sheet

SECTION III

1). Claim 18 relates to the treatment of human and/or animal bodies. According to Rule 67(1)(iv) an examination is not required for such a claim.

2). The Applicant is asked to explain the reason for the provisos found in claim 1. If they are intended to exclude some unacknowledged prior art known to the Applicant the said prior art should be cited and made available.

SECTION IV

1). Relevant prior art is represented by:

D1 WO-A-02/26722

2). An international patent application can contain only one invention or a plurality of inventions, if they are linked together by a single inventive concept.

In other word, there must be a specific technical feature common to all the claimed alternatives and which makes a contribution over the prior art taken as a whole.

Although all the claimed compounds seem to have a common pharmaceutical activity (antiinflammatory), a specific technical element shared by all the alternatives and making this contribution cannot be identified.

D1 discloses also compounds having the same pharmaceutical properties as those of the current application and (see example 60) discloses also compounds falling within the claimed scope.
It has to be noted that the mere disclaiming of such a compound cannot restore unity of invention.

The separate inventions/groups of invention are:

1. Claims 1-22 in which R^1 is imidazolyl
2. Claims 1-22 in which R^1 is triazolyl

3. Claims 1-22 in which R^1 is oxadiazolyl
4. Claims 1-22 in which R^1 is thiazolyl
5. Claims 1-22 in which R^1 is thiophenyl
6. Claims 1-22 in which R^1 is isoxadiazolyl
7. Claims 1-22 in which R^1 is isoxathiazolyl
8. Claims 1-22 in which R^1 is pyridinyl
9. Claims 1-22 in which R^1 is furanyl
10. Claims 1-22 in which R^1 is isoxazolyl
11. Claims 1-22 in which R^1 is tetrazolyl
12. Claims 1-22 in which R^1 is pyrazolyl

The applicant paid the corresponding fees for the inventions in which R^1 is furanyl, oxadiazolyl and pyrazolyl. This opinion is therefore limited to these subject-matters.

SECTION V

1). Relevant prior art is represented by:

D1 WO-A-02/26722
D2 EP-A-243959
D3 J.Med.Chem. (1991), vol. 34, p. 616-24
D4 WO-A-00/71518

2). The claimed matter is novel vis-à-vis D2 and D3, since the grouping "Y" is a single bond for the compounds disclosed in these documents.
The claimed matter is a selection vis-à-vis D4 but it is regarded as novel, since the specific combination of the structural elements of the claimed compounds is not disclosed in D4 (values of Y and values of R^1).

3). None of the cited documents discloses compounds having antiinflammatory properties as those currently claimed.

Thus, the problem underlying the current application appears to be the provision of further morpholinyl derivatives having antiinflammatory properties.

The data of the description show that this problem has been solved by some of the claimed

compounds.

In the absence of any relevant prior art, the skilled person would not arrive at the claimed compounds by using only his technical knowledge.

An inventive step is therefore not acknowledged on the whole claimed scope, since the wording of the claims contains expressions which are unlimited and therefore lead to an unlimited number of compounds which inherently cannot represent a solution to the given problem.

4). There is no objection with regard to industrial applicability.